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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/628,147	07/28/2003	Cameron M.L. Clokie	02738.0006.CNUS02	4385

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EXAMINER	
HENLEY III, RAYMOND J	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 10/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/628,147	CLOKIE, CAMERON M.L.	
	Examiner	Art Unit	
	Raymond J. Henley III	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 29-61 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 29-61 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 11/25/03.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

CLAIMS 29-61 ARE PRESENTED FOR EXAMINATION

Applicant's Preliminary Amendment filed July 28, 2003 and Information Disclosure Statement filed November 25, 2003 have been received and entered into the application. Accordingly, the specification at pages 1, 2, 7-10 and 13 has been amended; claims 1-28 have been canceled; and claims 29-61 have been added. Also, as reflected by the attached, completed copy of form PTO-1449, (2 sheets), the Examiner has considered the cited references.

Specification

The specification is objected to because of the following informalities. At page 1 of the specification, the identification of the parent application as "09/939,858", (emphasis added), should be corrected to read as ---09/939,898---. Also, the current status of this parent application as U.S. Patent No. 6,623,748 should be set forth.

Additionally, at page 4 of the present specification, lines 18 and 20, "osteoinductive" is erroneously duplicated. The second occurence of this term apparently should be changed to ---osteoconductive---.

Appropriate correction of the above is required.

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 29-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sander et al., (U.S. Patent No. 5,356,629, cited by Applicant in the IDS filed November 25, 2003 as reference "A4") in view of Schmolka, (see IDS filed November 25, 2003, reference C2), Lee et al., (U.S. Patent No. 7,026,292, cited by the Examiner), O'Leary et al., (U.S. Patent No. 5,290,558, cited by Applicant in the IDS filed November 25, 2003 as reference "A5"), Khor et al., (U.S. Patent No. 5,821,285, cited by the Examiner), Sanderson, (U.S. Patent No. 4,722,948, cited by the Examiner), Ducheyene et al., (U.S. Patent No. 5,817,327, cited by the Examiner) and Escobedo et al., (U.S. Patent No. 6,475,782, cited by the Examiner).

Sander et al. teach bone repair compositions comprising a bone powder material, (col. 4, lines 13-16), and a carrier comprising a solvent including water, and a Poloxamer or Pluronic-type polyoxyethylene-polyoxypropylene block co-polymer, (col. 5, lines 53-60). As the bone powder material, it is taught that such may be derived from xenograft bone, homologous bone, autogenous bone, (col. 4, lines 14-15), and as an osteoinductive agent, demineralized bone powder, moreslized cancellous bone, aspirated bone marrow or other autogenous bone sources, (col. 5, line 15). Sander et al. further teach that the composition comprises additional elements including a bioabsorbable, (a.k.a. biodegradable), polymeric material, (col. 3, lines 48-50 and 55-65), a biocompatible material such as hydroxyapatite, (col. 4, line 15), a therapeutic agent such as an antiobiotic, (col. 4, line 63), and one or several growth promoting factors such as osteoinductive protein, (i.e., a bone morphogenetic protein, (BMP); see Lee et al. at col. 5, lines 49-51, col. 6, lines 46-56 and col. 16, line 67 – col. 17, line 5). The Examiner deems the teaching of "hydroxyapatite" to represent a genus of sufficient scope so as to have placed the presently claimed concepts of "natural" or "synthetic" hydroxyapatite in the possession of the

public. Also, Sander et al. teach a method for effecting bone repair through implanting the above composition into a bone defect, (e.g., col. 1, lines 6-10, 57-59 and 65-68).

The differences between the above and the claimed subject matter lie in that Sander et al. fail to teach **(i)** the specific proportioning of ingredient amounts, (i.e., claims 37-39); **(ii)** the presently claimed terms "osteoconductive", "alloplastic", "xenogenic", allogenic", "autogenic" used to describe the presently claimed therapeutic materials; **(iii)** that the composition may comprise calcium carbonate, calcium phosphate, calcium sulfate, or combinations thereof, **(iv)** that the composition may comprise tissue growth factor beta, (TGF-β), bone morphogenic protein, (BMP), or both, including the specific species as set forth in the present claims, (e.g., claim 34), **(v)** PLURONIC™ F127, (a.k.a. poloxamer 407) as the specific block co-polymer, and **(vi)** that the composition may further comprise an analgesic, an anti-inflammatory agent and/or an agent to promote the development of a connective tissue or circulatory system tissue.

However, the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains because of the reasons which follows.

Regarding the amount of ingredients, including a polymer, contained in the composition, Sander et al. fail to specify specific proportions/concentrations. Rather, it is indicated that the composition, once introduced into the body, should be "moldable", (col. 5, lines 44, 51, and col. 6, line 3), "e.g., with a surgical spatula", (col. 5, line 67), as well as in "semi-solid form until suitable resorption of the matrix has taken place and/or regenerated bone tissue has been formed", (col. 6, lines 4-6). It is believed that one of ordinary skill in the art

could determine, through no more than necessary and routine experimentation, the specific proportioning of ingredients that would provide a composition having the above desired characteristics and that such proportioning is not patentably distinct from the presently claimed percentages.

Sander et al. teach the inclusion of specific compounds which Applicant has categorized as being "osteoconductive", "alloplastic", "xenogenic", allogenic", "autogenic", (e.g., hydroxyapatite or xenograft bone). That the patentees do not classify the compounds in the same manner as in the present claims is of no patentable moment, however, because such categories do not create compounds that would not have been obvious based on the teachings of Sander et al.

The addition of the presently claimed additional elements, (e.g., present claims 32, 33 and 44), such as TGF beta proteins, calcium carbonate, calcium sulfate, calcium phosphate, the specifically claimed TGF-β types, an analgesic, an anti-inflammatory, an agent to promote the development of a connective tissue or circulatory system tissue, such would have been obvious because in similar, bone-repair composition it was recognized that the addition of such agents was beneficial and as such, one of ordinary skill in the art would have been motivated to include such additional elements in the composition of Sander et al. in order to realize the art recognized benefits thereof.

In particular, Sander et al. further indicate that, in general, the incorporation of "one or more medico-surgically useful substances", (i.e., "substances which accelerate or beneficially modify the healing process when the composite is applied to the surgical repair site"), is beneficial, (col. 4, lines 51-55). In the art of bone repair compositions, such as those containing a bone material and a carrier, the addition of beneficial agents such as calcium carbonate,

calcium sulfate, calcium phosphate, (i.e., as fillers, see Khor et al. at col. 2, lines 53-65 or Sanderson at col. 12, claim 3), analgesics, antiinflammatory agents, (see Ducheyene et al. at col. 1, line 65 – col. 2, line 6), fibroblast, (a.k.a. connective tissue), growth factor, (Sander et al. at col. 5, line 1), and/or platelet derived growth factor, (Sander et al. at col. 5, lines 2-3; i.e., representing an agent to promote the development of a circulatory system tissue), was known which would have motivated one of ordinary skill in the art to select such beneficial agents given the general teaching of Sander et al. that additional beneficial agents could be employed. The Examiner has cited platelet derived growth factor as being representative of an agent to promote the development of a connective tissue or circulatory system tissue because Escobedo et al. indicate that this growth factor "stimulates migration of arterial smooth muscle cells from the medial to the intimal layer of the artery" which the Examiner interprets as a promotion of the development of a circulatory system tissue.

Also, Sander et al. teach the introduction of one or several growth promoting factors to promote repair and/or tissue growth, (col. 4, lines 67-68). Such factors include an osteogenic agent which stimulates or accelerates generation of bone upon implantation into a bone defect site and which agent may include osteoinductive protein, (col. 5, lines 11-15). One of ordinary skill in the art would have appreciated from the teaching of an osteoinductive protein by Sander et al. that BMP and/or TGF-β could be employed because both were known to be osteogenic proteins capable of inducing progenitor cells to form one or more tissue types including endochondral or intramembranous bone and cartilage. Indeed, as taught by Lee et al., the specifically claimed BMP compounds were known to be morphogenic and osteogenic compounds, (col. 16, line 59 – col. 17, line 5). Also, Lee et al. teach that the morphogenic

proteins employed for their osteogenic activity belong to the TGF-β protein superfamily, (col. 6, lines 46-48).

As noted above, Sander et al. do not specify PLURONIC™ F127, (a.k.a. poloxamer 407), as a specific co-polymer, (i.e., as in present claim 44). However, to one of ordinary skill in the art, PLURONIC™ F127 would have been an obvious PLURONIC™ co-polymer because Sander et al. teach Pluronic-type polyoxyethylene-polyoxypropylene block co-polymer in general, Schmolka establishes that the specific compound, poloxamer 407, was known, (see page 206, col. 2, first paragraph), and thus, in the absence of evidence to the contrary, the selection of any specific Pluronic-type polyoxyethylene-polyoxypropylene block co-polymer, including those polymers that inherently possessed differing rheological properties, (i.e., such as those that exhibit "reverse phase behavior when its temperature is increased from ambient to body temperature" as in present claim 1), from those known to the artisan would have been no more than an informed choice from effective alternatives.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting

ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 29-61 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over (i) claims 1-7 of Clokie, ("Clokie I", U.S. Patent No. 6,309,659, cited by Applicant in the IDS filed November 25, 2003 as reference "A13") or (ii) claims 1-8 of Clokie, ("Clokie II", U.S. Patent No. 6,623,748, cited by Applicant in the IDS filed November 25, 2003 as reference "A14"), in view of Sander et al., (U.S. Patent No. 5,356,629, cited by Applicant in the IDS filed November 25, 2003 as reference "A4"), Schmolka, (see IDS filed November 25, 2003, reference C2), Lee et al., (U.S. Patent No. 7,026,292), O'Leary et al., (U.S. Patent No. 5,290,558, cited by Applicant in the IDS filed November 25, 2003 as reference "A5"), Khor et al., (U.S. Patent No. 5,821,285, cited by the Examiner), Sanderson, (U.S. Patent No. 4,722,948, cited by the Examiner), Ducheyene et al., (U.S. Patent No. 5,817,327, cited by the Examiner) and Escobedo et al., (U.S. Patent No. 6,475,782, cited by the Examiner).

Although the conflicting claims are not identical, they are not patentably distinct from each other because central to both the subject matter as presently claimed and as claimed in either Clokie I or II is a biocompatible tissue repair composition comprising a bone powder, such as a demineralized bone powder, and a carrier that exhibits reverse phase behavior when its temperature is increased from ambient to body temperature, such as the poly(oxyalkylene) block copolymer PLURONIC™ F127, (a.k.a. poloxamer 407) and water. While the present claims require the inclusion of additional elements not recited in the patented claims, the claims are not patentably distinct because, given that the patented claims recite "comprising", in practicing the

subject matter of the present claims, one would be practicing or anticipating the subject matter of the patented claims. That is, the term "comprising" of the patented claims allows for the un-recited additional elements of the present claims.

Alternatively, the presently claimed subject matter would have been obvious from the patented claims in view of Sander et al. Sander et al. teach bone repair compositions analogous to that which is claimed in either Clokie I or II in that Sander et al. disclose bone repair composition comprising a material derived from a bone powder material, (col. 4, lines 13-16), and a carrier comprising a Poloxamer or Pluronic-type polyoxyethylene-polyoxypropylene block co-polymer, (col. 5, lines 53-60). Sander et al. do not specify PLURONIC™ F127, (a.k.a. poloxamer 407), as a specific co-polymer, (i.e., as in present claim 44). However, to one of ordinary skill in the art, PLURONIC™ F127 would have been obvious because Sander et al. teach Pluronic-type polyoxyethylene-polyoxypropylene block co-polymer in general, Schmolka establishes that poloxamer 407 was known, (see page 206, col. 2, first paragraph), and thus, in the absence of evidence to the contrary, the selection of any specific Pluronic-type polyoxyethylene-polyoxypropylene block co-polymer, including those polymers that inherently possessed differing rheological properties, (i.e., such as those that exhibit "reverse phase behavior when its temperature is increased from ambient to body temperature" as in present claim 1), from those known to the artisan would have been no more than an informed choice from effective alternatives.

Sander et al. further teach the addition of such additional elements to the bone repair composition as a bioabsorbable, (a.k.a. biodegradable), polymeric material, (col. 3, lines 48-50 and 55-65), biocompatible material such as hydroxyapatite, (col. 4, line 15), a therapeutic agent

such as an antibiotic, (col. 4, line 63), and one or several growth promoting factors such as osteoinductive protein, (i.e., a bone morphogenetic protein, (BMP); see Lee et al. at col. 5, lines 49-51, col. 6, lines 46-56 and col. 16, line 67 – col. 17, line 5). The Examiner deems the teaching of "hydroxyapatite" to represent a genus of sufficient scope, (i.e., respecting the origin of the material), such that one of ordinary skill in the art would have immediately envisaged the presently claimed concepts of "natural" or "synthetic" hydroxyapatite.

While Sander et al. do not highlight the presently claimed specific proportioning of ingredients, (e.g., claims 37-39), or the addition of the presently claimed additional elements, (e.g., present claims 32, 33 and 44), such as TGF beta proteins, calcium carbonate, calcium sulfate, calcium phosphate, the specifically claimed tissue growth factor beta (TGF-β) types, an analgesic, an antiinflammatory, an agent to promote the development of a connective tissue or circulatory system tissue, such would have been obvious because in similar, bone-repair composition it was recognized that the addition of such agents was beneficial and as such, one of ordinary skill in the art would have been motivated to include such additional elements in the composition of Sander et al.

In support of the above conclusion of obviousness, the Examiner relies on Lee al. at col. 6, lines 46-49 where it is taught that the morphogenic proteins employed in their invention belong to the TGF-β protein superfamily thus indicating that both known morphogenic proteins and TGF-β proteins could themselves be employed. The selection of any particular morphogenic proteins or TGF-β proteins from those known would have been a matter well within the purview of one of ordinary skill in the art.

Sander et al. also indicate that, in general, the incorporation of "one or more medico-surgically useful substances", (i.e., "substances which accelerate or beneficially modify the healing process when the composite is applied to the surgical repair site"), is beneficial, (col. 4, lines 51-55). In the art of bone repair compositions, such as those containing a bone material and a carrier, the addition of beneficial agents such as calcium carbonate, calcium sulfate, calcium phosphate, (i.e., as fillers, see Khor et al. at col. 2, lines 53-65 or Sanderson at col. 12, claim 3), analgesics, antiinflammatory agents, (see Ducheyene et al. at col. 1, line 65 – col. 2, line 6), fibroblast, (a.k.a. connective tissue), growth factor, (Sander et al. at col. 5, line 1), and/or platelet derived growth factor, (Sander et al. at col. 5, lines 2-3), was known which would have motivated one of ordinary skill in the art to select such beneficial agents given the general teaching of Sander et al. that additional beneficial agents could be employed. The Examiner has cited platelet derived growth factor as being representative of an agent to promote the development of a connective tissue or circulatory system tissue because Escobedo et al. indicate that this growth factor "stimulates migration of arterial smooth muscle cells from the medial to the intimal layer of the artery" which the Examiner interprets as a promotion of the development of a circulatory system tissue.

Regarding the amount of polymer contained in the composition, Sander et al. fail to specify specific proportions/concentrations. Rather, it is indicated that the composition, once introduced into the body, should be "moldable", (col. 5, lines 44, 51, and col. 6, line 3), "e.g., with a surgical spatula", (col. 5, line 67), as well as in "semi-solid form until suitable resorption of the matrix has taken place and/or regenerated bone tissue has been formed", (col. 6, lines 4-6). It is believed that one of ordinary skill in the art could determine, through no more than

necessary and routine experimentation, the specific proportioning of ingredients that would provide a composition having the above desired characteristics.

Accordingly, for the above reasons, the claims are deemed properly rejected.

None of the claims are currently in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond J. Henley III whose telephone number is 571-272-0575. The examiner can normally be reached on M-F, 8:30 am to 4:00 pm Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Raymond J Henley III
Primary Examiner
Art Unit 1614

September 29, 2006